

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

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| Date of mailing (day/month/year) 22 FEB 2005 | | |
| FOR FURTHER ACTION See paragraph 2 below | | |
| Applicant's or agent's file reference 08321-0136PC | | |
| International application No. PCT/US04/23848 | International filing date (day/month/year) 26 July 2004 (26.07.2004) | Priority date (day/month/year) 08 August 2003 (08.08.2003) |
| International Patent Classification (IPC) or both national classification and IPC IPC(7): C12Q1/68; C07H 21/04, 21/02 and US Cl.: 435/6; 536/23.1, 24.3, 24.32, 24.33 | | |
| Applicant THOMAS JEFFERSON UNIVERSITY | | |

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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| Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230 | Authorized officer <i>Marc J. Wilder</i> Cynthia B. Wilder, Ph.D. Telephone No. (571) 272-1600 |
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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/23848

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☒ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☒ in written format

☒ in computer readable form

c. time of filing/furnishing

☒ contained in international application as filed.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US04/23848

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

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|-------------------------------|-------------------------------|-----|
| Novelty (N) | Claims <u>1-40, and 42-44</u> | YES |
| | Claims <u>41</u> | NO |
| Inventive step (IS) | Claims <u>1-40 and 42-44</u> | YES |
| | Claims <u>41</u> | NO |
| Industrial applicability (IA) | Claims <u>1-44</u> | YES |
| | Claims <u>NONE</u> | NO |

2. Citations and explanations:

Claim 41 lacks novelty under PCT Article 33(2) as being anticipated by Rothschild et al. Regarding claim 41, Rothschild teaches a product or kit comprising at least two different selectable tags and corresponding affinity media, a single stranded DNA binding reagent and linking moiety (see col. 9-14, 18, 23-25 and 49-50). Therefore, Rothschild meets the limitations of the instant invention of claim 41.

Claims 1-40 and 42-44 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest a method of identifying an alternatively spliced RNA molecule in conjunction with a normally spliced counterpart RNA using a selectable tag comprising an oligonucleotide having a longer and shorter strand each with a 5' end that when annealed form a six base pair double stranded region and an 11 base 5' single stranded overhang, and wherein a biotin molecule is attached to the 5' end of the longer oligonucleotide strand and the 5' end of shorter oligonucleotide strand is phosphorylated at the 5' end and wherein the 11 base 5' overhang comprises a six base nucleotide sequence which when annealed with a single stranded oligonucleotide comprising the complementary sequences forms a Sma I or PmlI restriction site. The prior art also does not teach a polynucleotide linking moiety comprising SEQ ID NO: 5.

The closest prior art, Schweighoffer et al teach a method of identifying an alternatively spliced RNA molecule in conjunction with a normally spliced counterpart RNA using forming a population of cDNAs, cross-hybridizing and identifying or cloning hybridids formed in a population of nucleic acid comprising unpaired regions corresponding to portions of genes that are differentially spliced between said samples.

Carninci et al teach a sequence having 47.6% sequence homology to the sequence of SEQ ID NO: 5.

Rothschild et al teach selectable tags comprising and oligonucleotide and biotin.

Claims 1-44 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.